REMARKS

Claims 3 and 5-16 are pending in the present application.

Applicants wish to thank Examiner Friend for the helpful and courteous discussion with their undersigned Representative on February 20, 2003. Applicants also would like to thank Examiner Friend for the indication that the previous rejections of Claims 2-4, objections to the specification, and objections to the claims have been withdrawn (see paper number 14, page 3, lines 16-25).

The rejection of Claims 2-13 under 35 U.S.C. §112, first paragraph ("written description") is traversed.

The Office has alleged that the specification fails to meet the written description requirement of 35 U.S.C. §112, first paragraph (paper number 14, page 5). Applicants respectfully disagree.

The Office asserts that the specification fails to provide a sufficient description of the scope of the drug and/or protein targeted by the drug. To support this assertion, the Office notes that "it is a well-established fact in the art of pharmaceuticals, that even a small change in the structure of a drug often renders the drug unable to bind its corresponding protein target(s)" (paper number 14, page 5, lines 27-28). The Office further states that the *only* way to demonstrate possession of the full scope of the claimed method is that "applicants must provide representative examples that would reasonabl[y] convey to one skilled in the art that applicants, at the time of filing, possessed a method that would work with most drug/crosslinker/antigenic substance combination" (paper number 14, page 6, lines 2-5). However, Applicants direct the Examiner's attention to MPEP §2163.02:

> An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

Applicants submit that this objective standard has been met by the present specification. Specifically, Applicants claim a general method for in vitro detection of a gene encoding a drug-targeted protein. As stated on page 3, lines 10-16, the drug is defined as being suitable for administration to a living organism, which non-protein and has no per se antigenicity. Further, on page 4, lines 1-7, Applicants discuss the relevance and necessity of having or introducing a functional group that is compatible with the selected cross-linker, as well as the need to conserve the efficacy of the drug when coupled with the cross-linker. The structure of the drug itself is not particularly relevant, so long as it meets these criteria outlined above. Moreover, the proteins that are targeted by the drug that is selected is directly correlated to the drug selected and since the claimed method seeks to identify these very proteins, the Examiner's objection based on the lack of recited structure, function, or cellular location is of no moment.

At page 6, lines 2-5 of paper number 14, the Examiner has apparently taken the position that the data presented by Applicants is insufficient to establish the written description of the claimed invention. Applicants note that the written description requirement does not carry with it a requirement for submission of experimental data. Instead, as stated above, the question that is relevant to compliance with the written description requirement of 35 U.S.C. 112, first paragraph, is that defined in MPEP §2163.02, which Applicants have met.

Therefore, the present claims do clearly allow the skilled artisan to recognize what has been invented and what is claimed is adequately described in the specification within the

meaning of 35 U.S.C. §112, first paragraph. Accordingly, withdrawal of this ground of rejection is requested.

The rejection of Claims 2-14 under 35 U.S.C. §112, first paragraph ("enablement"), is traversed.

The Examiner asserts that the arguments presented in the Amendment and Request for Reconsideration filed on May 8, 2002 do not address the factors cited by the Examiner in paper number 6, which were used as a basis for determining whether undue experimentation would be required. However, Applicants disagree with this assertion as well as the conclusion drawn therefrom.

In re Wands factors may be a general guideline for ascertaining compliance with the enablement requirement of 35 U.S.C. §112, first paragraph; however, as set forth in MPEP §2164.04:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Applicants have duly responded to the In re Wands factors by specifically demonstrating how the present application is in full compliance with the MPEP §2164.04. Specifically, at page 3, lines 9-15, the Applicants define the preferred drugs that may be used as a component of the probe. At page 3, lines 18 through page 4, line 7, the Applicants provide guidance for the selection of suitable cross-linkers, complete with a list of preferred examples, to tether the drug to the antigenic substance. Further, at page 4, lines 8-22, the Applicants provide a detailed description of suitable antigenic substances, which has now been defined in Claim 5 to be either serum albumin or fluorescein isothiocyanate. Moreover,

at page 4, lines 23-27, page 6, lines 1-5, and page 6, line 14 to page 7, line 5, the Applicants provide explanations of how to make the claimed compounds. Not only do the Applicants provide adequate disclosure to fully enable the skilled artisan to make the claimed compounds, Applicants have provided a screening method to enable the skilled artisan to assess the effectiveness of the compounds made thereby (page 7, line 6 to page 10, line 13). Therefore, the Applicants have met their burden of clearly defining the scope of the claimed compounds, how to make the compounds, and how to use the compounds.

In fact, MPEP §2164.06 states:

> ... quantity of experimentation needed to be performed by one skilled in the art is only one factor involved in determining whether "undue experimentation" is required to make and use the invention. "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." In re Colianni, 561 F.2d 220, 224, 195 USPQ 150, 153 (CCPA 1977). " 'The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.

Applicants submit that, with the present specification in hand, determination of the specific drug/cross-linking agent/antigenic substance (i.e., serum albumin or fluorescein isothiocyanate) combinations that fall within the scope of the present invention would require nothing more than routine experimentation. As such, Applicants submit that the claims of the present application are fully enabled within the context of 35 U.S.C. §112, first paragraph.

The MPEP further states in §2164.02:

> The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation.

Despite fully enabling the artisan to practice the present invention, even in the absence of a working example, Applicants provide an extremely detailed Example (pages 6-10) to help guide the artisan to practice the present invention.

Accordingly, this ground of rejection is believed to be unsustainable and its withdrawal is requested.

The rejection of Claims 2-13[1] under 35 U.S.C. §102(b) over Sparks et al is traversed.

Sparks et al disclose a method of identifying polypeptides having functional domains of interest (and DNA sequences encoding the same), by means of a sequence-independent, recognition unit-based functional screen (see Abstract). As the Examiner points out, Sparks et al disclose avidin or streptavidin as their "antigenic substance" (see page 33, lines 13-17).

However, in present Claim 5 the antigenic substance is defined as being either serum albumin or fluorescein isothiocyanate (see Claim 5). Applicants note that Sparks et al fail to disclose or suggest either of these antigenic substances and, as such, this reference fails to anticipate the present invention.

Moreover, Applicants submit that the present invention would not even be obvious in view of the disclosure of Sparks et al. Specifically, as defined in present Claim 5 screening for the gene encoding a protein targeted by said drug is accomplished by *using an antigen-antibody reaction* between the antigenic substance of the probe and a labeled antibody specific for the antigenic substance. This method is in direct contrast to the method of Sparks et al, which employs a direct biotin/avidin (or streptavidin) interaction rather than an antigen/antibody interaction.

Accordingly, Applicants request withdrawal of this ground of rejection.

The rejection of Claims 2-12 under 35 U.S.C. §103(a) over Sparks et al and Hutchins et al is traversed.

Sparks et al is discussed above. Hutchens et al disclose water production from a wellbore by injection of a hydrophilic polymer-containing organic carrier fluid and a crosslinking agent-containing fluid into at least a portion of a subterranean formation (see Abstract).

At the outset, Applicants note that the mere fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness (MPEP §2143.01). To satisfy the motivation to combine requirement, the Examiner points to the "catch-all" phrase by Sparks et al to use "known cross-linking reagents. " However, this suggestion by Sparks et al lacks the necessary particularity to motivate the artisan to reach outside of the realm of analogous art (i.e., phage display and high-throughput detection of drug-targeted proteins) to the field of oil and gas extraction from subterranean formations (Hutchins et al).

Even if the artisan would ever, even inadvertently, combine the teachings of Sparks et al and Hutchins et al this combination would fail to render the present invention obvious. Specifically, as stated above, Sparks et al fail to disclose or suggest using either of the antigenic substances defined in Claim 5 (i.e., serum albumin or fluorescein isothiocyanate). Hutchins et al do not compensate for this deficiency in the disclosure of Sparks et al and, as such, the present invention would not be obvious in view of this combination of references.

Therefore, Applicants request withdrawal of this ground of rejection.

[1] Also listed on page 8, lines 9-10 of the paper number 14 as claims 5, 2-4, 6-8, 11, and 12

The rejection of Claims 2-13 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Regarding points (A), (B), (C), and (E), Applicants note that the claims have been amended to remove and/or clarify the language that the Examiner has found objectionable.

With respect to the Examiner's point (D), Applicants submit that Claim 5 has been amended to clearly define the essential steps of the inventive method. Specifically, Claim 5 provides a method for in vitro detection of a gene encoding a drug-targeted protein, by (a) making a probe by linking an antigenic substance to a drug via a chemical cross-linker to form a probe, (b) screening for the gene encoding a protein targeted by said drug, wherein said protein is expressed from a cDNA expression library containing genes of an organism to which the drug is to be administered, by using an antigen-antibody reaction between the antigenic substance of the probe and a labeled antibody specific for the antigenic substance; and (c) determining the gene sequence of the protein expressed from the cDNA expression library contained within the probe-bound phage.

MPEP §2171 sets for the following two separate requirements under 35 U.S.C. §112, second paragraph:

> (A) the claims must set forth the subject matter that applicants regard as their invention; and
>
> (B) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Moreover, MPEP §2173.02 states:

> The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph is whether the claim meets the threshold requirements of clarity and precision...

Applicants submit that Claim 5 as currently presented clearly meets these the requirements set forth above and as such meets the requirements of 35 U.S.C. §112, second paragraph.

Applicants request withdrawal of this ground of rejection.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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